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 >>>Duplicate detection is not supported for File 393.
 >>>Duplicate detection is not supported for File 391.
 >>>Records from unsupported files will be retained in the RD set.
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                                                               3 RD (unique items)
 ? t s51/3, k/1-3
 >>>KWC option is not available in file(s): 399
 51/3, K/1 (Item 1 from file: 399)
DIALOG(R) File 399: CA SEARCH(R)
 (c) 2010 American Chemical Society. All rts. reserv.
         144127496
                                                               CA: 144(8) 127496p
                                                                                                                                                       PATENT
         Treatment of bacterial infections via inhibition of acetyl-CoA
         acet yltransferase
         INVENTOR(AUTHOR): Burnie, James Peter; Matthews, Ruth Christine; Carter,
 Tracey
        acey
LCCATI CN: UK,
ASSIGNEE: Neutec Pharma PLC
ASSIGNEE: 
        PALEST CATIONS (2) 200507426 A1 DATE: 20060112 APPLICATION: W0 20050262607 (20050701) *08 200414886 (20040702) PATENT CLASSIFICATIONS: CLASSIF
                 CLASS: C07K- 016/ 12A; A61K- 039/ 395B
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Page 1

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51/3, K/2 (Item 2 from file: 399)
DIALOG(R) File 399: CA SEARCH(R)
(c) 2010 American Chemical Society, All rts, reserv.
                     CA: 141(24)394083q
                                                     PATENT
   Antibody repertoire against Clostridium difficile
   INVENTOR(AUTHOR): Burnie, James Peter; Matthews, Ruth Christine
   LOCATION: UK.
   ASSIGNEE: Neutec Pharma PLC
PATENT: PCT international; WO 200494474 A1 DATE: 20041104
APPLICATION: WO 2004GB1619 (20040414) * GB 20039126 (20030417)
   PAGES: 91 pp. CODEN: F
PATENT CLASSIFICATIONS:
                       CODEN: PIXXD2 LANGUAGE: English
      CLASS: C07K-016/12A;
                                    A61K-039/40B: C12Q-001/68B: Q01N-033/563B
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 51/3. K/3
DIALOG(R) File 399: CA SEARCH(R)
(c) 2010 American Chemical Society. All rts. reserv.
   141291235
                     CA: 141(18)291235m
                                                     PATENT
   Protein and cDNA sequences of a novel Clostridium difficile lactate
   dehydrogenase and diagnostic and therapeutic use for bacterial infection
   INVENTOR (AUTHOR): Burnie, James Peter: Matthews. Ruth Christine
   LOCATION: UK,
   ASSI ONEE: Neutec Pharma PLC
PATENT: PCT International: WO 200485637 At DATE: 20041007
APPLICATION: WO 2004081383 (20040325) "GB 20036782 (20030325)
   PAGES: 42 pp. CODEN: PIXXD2 LANGUAGE: English PATENT CLASSIFICATIONS:
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? e au=matthews, ruth
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      Items Index-term
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8 AU=MATTHEWS, RUTH C
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>>>Duplicate detection is not supported for File 393.
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>>>Records from unsupported files will be retained in the RD set.
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? t s54/3, k/1-4
>>>KW C option is not available in file(s): 399
54/3, K/1 (Item 1 from file: 399)
DIALOG(R) File 399: CA SEAROH(R)
(c) 2010 American Chemical Society. All rts. reserv.
                                        PATENT
  144127496
                 CA: 144(8) 127496p
  Treatment of bacterial infections via inhibition of acetyl-CoA
  acet vitransferase
  INVENTOR(AUTHOR): Burnie, James Peter: Matthews, Ruth Christine: Carter,
Tr acey
  ACCATION: UK,
ASSI GNEE: Neutec Pharma PLC
PATENT: PCT International; WD 200603426 A1 DATE: 20060112
APPLICATION: WD 2005@2607 (20050701) *@ 200414886 (20040702)
  PACES: 59 pp. CODEN: F
PATENT CLASSIFICATIONS:
                 CODEN: PIXXD2 LANGUAGE: English
    CLASS: C07K-016/12A; A61K-039/395B
  DESIGNATED COUNTRIES: AE; AG, AL; AM, AT; AU; AZ; BA; BB; BG, BR; BW, BY;
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54/3, K/2 (Item 2 from file: 399)
DIALOG(R) File 399: CA SEARCH(R)
(c) 2010 American Chemical Society. All rts. reserv.
                              CA: 141(24)394083q
                                                                               PATENT
    141394083
    Antibody repertoire against Clostridium difficile
    INVENTOR (AUTHOR): Burnie, James Peter: Matthews, Ruth Christine
    LOCATION: UK.
    ASSIGNEE: Neut ec Pharma PLC
    PATENT: PCT international; WO 200494474 A1 DATE: 20041104
APPLI CATI CN: WO 2004@81619 (20040414) © 20 20039126 (20030417)
PAGES: 91 pp. CODEN: PIXXIOZ LANGUIAGE: English
    PAGES: 91 pp. CODEN: F
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54/3, K/3 (Item 3 from file: 399)
DIALOG(R) File 399: CA SEAROH(R)
(c) 2010 American Chemical Society. All rts. reserv.
                              CA: 141(18) 291235m
                                                                            PATENT
    141291235
    Protein and cDNA sequences of a novel Clostridium difficile lactate
    dehydrogenase and diagnostic and therapeutic use for bacterial infection
    INVENTOR (AUTHOR): Burnie, James Peter: Matthews, Buth Christine
    LOCATION: UK,
    ASSIGNEE: Noutec Pharma PLC
PATENT: PCT International; WO 200485637 A1 DATE: 20041007
APPLICATION: WO 2004691383 (20040325) *GB 20036782 (20030325)
PAGES: 42 pp. CODEN: PIXXD2 LANGUAGE: English
    PAGES: 42 pp. CODEN: F
PATENT CLASSI FI CATI ONS:
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54/3, K/4 (Item 4 from file: 399)
DIALOG(R) File 399: CA SEARCH(R)
(c) 2010 American Chemical Society, All rts, reserv.
                CA: 105(15)131784t
  105131784
                                          JOURNAL
  Immunoblotting to demonstrate antigenic and immunogenic differences among
  nine standard strains of Clostridium difficile
  AUTHOR(S): Heard, Shelley R.: Pasburn, Barbara: Matthews, Ruth C.:
Tabaqchall, Soad
LCCATION: Dep. Med. M.crobiol., St. Bartholomew's Hosp. Med. Coll.,
London, UK, EČÍA 7BE
JOURNAL: J. Clin. M. crobiol. DATE: 1986 VOLUME: 24 NUMBER: 3 PAGES:
384-7 CODEN: JCM DW ISSN: 0095-1137 LANGLAGE: English
?'s clostridium and (lactate and dehydrogenase)
290576 CLOSTRIDIUM
           675628 LACTATE
          1225788 DEHYDROGENASE
               935 CLOSTRI DI UM AND (LACTATE AND DEHYDROGENASE)
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             95957
                     DIFFICILE
               154 S55 AND DIFFICILE
      S56
? rd
>>>Duplicate detection is not supported for File 393.
>>>Duplicate detection is not supported for File 391.
>>>Records from unsupported files will be retained in the RD set.
                71 RD (unique items)
? s s57 and (immunogen or antigen?)
71 S57
             46199 I MM INCOFN
          5661503 ANTI ŒN?
                26 S57 AND (IMMUNOGEN OR ANTIGEN?)
      S58
? rd
>>>Duplicate detection is not supported for File 393.
>>>Duplicate detection is not supported for File 391.
>>>Records from unsupported files will be retained in the RD set.
      S59
                26 RD (unique items)
? t s59/3, k/1-26
>>>KWC option is not available in file(s): 399
59/3, K/1 (Item 1 from file: 34)
DIALOG(R) File 34: Sci Search(R) Cited Ref Sci
(c) 2010 The Thomson Corp. All rts. reserv.
20704114
             Genuine Article#: 603XQ No. References: 42
Title: The Effects of Substituted Cyclodextrins on the Colloidal and
    Conformational Stability of Selected Proteins
Author: Samra HS (REPRINT); He F; Bhambhani A; Pipkin JD; Zimmerer R;
    Joshi SB; Middaugh CR
Corporate Source: Univ Kansas, Dept Pharmaceut Chem, Macromol & Vaccine Stabilizat Lab, Lawrence//KS/66047 (REPRINT); Univ Kansas, Dept
    Phar maceut Chem, Macromol & Vaccine Stabilizat Lab, Lawrence//KS/66047;
    OvDex Pharmaceut Inc. Lenexa//KS/66214
Journal: JOURNAL OF PHARMACEUTICAL SCIENCES, 2010, V99, N6 (JUN). P
    2800-2818
I SSN: 0022-3549
                   Publication Date: 20100600
```

Page 5

10550410, t xt Digital Object Identifier: 10.1002/jps.22053 Publisher: JOHN WILEY & SONS INC. 111 RIVER ST, HOBOKEN, NJ 07030 USA Funding: The authors would like to thank Dr. Wendy L. Picking for the expression and purification of the LcrV used in the study. We also are grateful to Acambis, Inc. (Cambridge, MA) for providing Toxoid A and Human Genome Sciences, Inc. (Rockville, MD) for providing FGF-10. The study was financially supported by CyDex Pharmaceuticals. Inc. (Lenexa, KS). Funding Organization -- Grant Number: OvDex Pharmaceuticals, Inc. (Lenexa, KS) Document Type: ARTI CLE (ABSTRACT AVAI LABLE) Language: English ... Abstract: mechanism by which cyclodextrins stabilize proteins. The three proteins examined in this study are the Clostridium difficile Toxoid A, Yersinia pestis low-calcium response V or V antigen (Lcry), and fibroblast growth factor 10 (FGF-10). These three pharmaceutically relevant proteins differ in... ... Identifiers: ETHER BETA-CYCLODEXTRINS: FIBROBLAST-GROWTH-FACTOR: PHARMACEUTI CAL APPLICATIONS; INCLUSION COMPLEXATION; LACTATE-DEHYDROCENASE; THERWAL-STABILITY; ACCRECATION; BINDING EXCI PI ENTS: 2- HYDROXYPROPYL- BETA- CYCLODEXTRI N 59/3, K/2 (Item 1 from file: 72) DIALCO(R) File 72: EMBASE (c) 2010 Elsevier B. V. All rts. reserv. 0081025265 EMBASE/ Medline No: 2006085246 Safety, pharmacokinetics and influence on the intestinal flora of BAY 12-8039 (moxifloxacin hydrochloride) after oral administration in healthy male subjects Chnishi A.; Toyoki T.; Yoshikawa K.; Hashizume K.; Tanigawa T.; Tanaka T. Komori T. Department of Internal Medicine, Jikei University School of Medicine CORRESP. AUTHOR/AFFIL: Chnishi A.: Department of Internal Medicine, Jikei University School of Medicine Japanese Pharmacology and Therapeutics (Jpn. Pharmacol. Ther.) (Japan) December 1, 2005, 33/10 (1029–1045) CODEN: YACHD | SSN: 0386-3603 DOCUMENT TYPE: Journal; Article LANGUAGE: Japanese SUMMARY LAN RECORD TYPE: Abstract SUMMARY LANGUAGE: English; Japanese NUMBER OF REFERENCES: 33 ... weeks after the final dose. There were no changes in aerobes and fungi. In addition, Clostridium difficile D-1 antigen was not found. Conclusion: Single or al doses of 100 mg to 600 mg and multiple DRUG DESCRIPTORS: al ani ne ami not ransferase--endogenous compound--ec: aspartate am not ransferase -- endogenous compound -- ec; I act at e dehydrogenase--endogenous compound--ec; placebo; triacyl glycerol l i pase--endogenous compound--ec MEDI CAL DESCRI PTORS: ... CAS REGISTRY NO.: 9014-30-6 (alanine aminotransferase); 9000-97-9 (aspartate aminotransferase); 9001-60-9 (lactate dehydrogenase); 151096-09-2 (moxifloxacin); 9001-62-1 (triacylglycerol lipase)

59/3, K/3 (Item 2 from file: 72) DIALOG(R) File 72: EMBASE

```
(c) 2010 Elsevier B. V. All rts. reserv.
0078596071
                    EMBASE/ Medl i ne No: 2001202372
Intravascular large B-cell lymphoma or intravascular lymphomatosis:
Report of a case diagnosed by testicle biopsy
   Van Droogenbroeck J.; Altintas S.; Pollefliet C.; Schrovens W.: Berneman
   Department of Hematology, University Hospital Antwerp, Wilrijkstraat 10,
  2650 Edegem, Belgium
CORRESP. AUTHOR/AFFIL: Van Droogenbroeck J.: Department of Hematology,
University Hospital Antwerp, Wirijkstraat 10, 2650 Edegem, Belgium
CORRESP. AUTHOR EMALL: jan.van.droogenbroeck@uza.uia.ac.be
   Annals of Hematology (Ann. Hematol.) (Germany) June 29, 2001, 80/5
   (316-318)
CODEN: ANHEE
                       I SSN: 0939-5555
   DOI: 10.1007/s002770000268
  DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract
LANGUAGE: English SUMMARY LANGUAGE: English
NUMBER OF REFERENCES: 20
DRUG DESCRIPTORS:
...ampxicillin plus clavulanic acid--intravenous drug administration--iv: C
reactive protein--endogenous compound--ec; CD5 antigen--endogenous compound--ec; cefepime--drug therapy--dt; cycl ophosphamide--drug
combination -- cb; cycl ophospham de--drug therapy--dt...
... hemogl obi n--endogenous compound--ec; immunogl obul in G--endogenous
compound--ec: immunoglobulin kappa chain--endogenous compound--ec:
Lact at e dehydrogenase--endogenous compound--ec;
met hyl prednisol one--intravenous drug administration--iv; metronidazole
--drug therapy--dt; prednisolone--drug combination...
...blood culture; cancer combination chemotherapy; Candida albicans;
candid lasis-drug therapy-dt; case report; clinical examination;
Costridium difficile; echography; edema; Enterobacter cloacae;
epididymitis; human; hypoal bum nemia; interstitial pneumonia; lactate
dehydrogenase blood level; lethargy; male; monoclonal dehydrogenase blood level; lethargy; male; monoclonal immunoglobul inmedia; priority journal; pyrexia diopathica; sweating ... CAS FEG STRY NO.: 73-4 ([luconazole]): 9005-02-0 (hemoglobin): 97794-27-9
     (immunoglobulin G; 9001-60-9 (lactate dehydrogenase);
     6923-42-8...
59/3, K/4 (Item 3 from file: 72)
DIALOG(R) File 72: EMRASE
(c) 2010 Elsevier B.V. All rts. reserv.
0075821767
                    EMBASE/ Medl i ne No: 1994253272
   Infusional cyclophosphamide, doxorubicin and etoposide in HIV-related
non-Hodgkin's Tymphosma. A follow up report of a highly active regimen
Sparano J.A.; Wernik P.H.; Strack M; Leaf A; Becker N.H.; Sarta C.;
Carney D.; Ekind R; Shah M; Valentine E.S.; Dutcher J.P.
   Albert Einstein Cancer Center, Montefiore Medical Center, 111 East 210th
   Street, Bronx, NY 10467, United States
   CORRESP. AUTHOR/AFFIL: Sparano J.A.: Albert Einstein Cancer Center
Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467, United
States
   Leukemia and Lymphoma ( LEUK, LYMPHOMA ) (United Kingdom) August 18.
   1994, 14/3-4 (263-271)
CODEN: LELYE ISSN: 1
                      I SSN: 1042-8194
```

Page 7

DOCUMENT TYPE: Journal; Article RECORD TYPE: Oitation

LANGUAGE: English SUMMARY LANGUAGE: English

DRUG DESCRI PTORS:

cd4 antigen; cd8 antigen MEDICAL DESCRIPTORS:

MEDICAL DESCRIPTIONS: adult; article; aspergillosis--side effect--si; blood toxicity--side effect --si; clinical article; clostridium difficile; colitis--side effect--si; drug efficacy; female; fever--side effect--si; follow up; herpes labialis--side effect--si; human; human immunodeficiency virus

herpes labialis-side effect-si; human; human immunodefici infection; intravenous drug administration; lactate

dehydrogenase blood level; lymphocyte count; male; meningitis; neutropenia--side effect--si; opportunistic infection--side effect--si...

59/3, K/5 (Item 1 from file: 135) DIALOQ(R) File 135: News Rx Weekly Reports (c) 2010 News Rx. All rts. reserv.

0000419002 (USE FCHMAT 7 OR 9 FCR FULLTEXT) Recent research focus of reports from University of Pittsburgh, U.S. Pharma Business Wek, January 22, 2007, p. 1064

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English

RECORD TYPE: FULLTEXT WORD COUNT: 1041

... for nuclear viability. This was accompanied by little or no protection against 6-hydroxydopamine-induced lactate dehydrogenase release, decline in ATP, or reduction in (3)H-dopamine uptake. The antioxidant, N-acetvi...

. . S.

Study 2: According to a study from the United States, ozone (O) exposure impairs antigen-specific immunity but activates interleukin (IL)-7-induced proliferation of CD4-CD8- thymocytes in balb...

...killer (NK) cell activity and the proliferation potential of spleen T cells to a specific antigen stimulus. Immunological function assays indicated that O-3 exposure attenuated the proliferation of spleen mononuclear...

...in this mouse model."

Feng and colleagues published their study in the (Ozone exposure impairs antigen-specific immunity but activates IL-7-induced proliferation of CO4-CD8- thymocytes in balb/c...

DESCRIPTORS:

Clostridium difficile; Diagnostics; Environment; Environmental Health; Cenotyping; Nosocomial Transmission; Pennsylvania; Pittsburgh; U S; United States; University of...

59/3, K/6 (Item 1 from file: 357) DIALOG(R) File 357: Derwent Biotech Res. (c) 2010 Thomson Reuters. All rts. reserv.

0.465554 DBR Accession No.: 2009-11190 PATENT

New vaccine composition comprises immune stimulating complex, saccharide antigen and aluminum containing adjuvant, used for preparing medicament for treating clinical condition, e.g. bacterema, meningitis, and pneumonia, in an individual - pharmaceutical composition comprising immune stimulating complex, saccharide antigen and aluminum containing adjuvant, useful as vaccine for Page 8

treatment and prevention of bacteraema, meningitis and pneumonia AUTHOR: KIRKBYN S; SCHICETTA

PATENT ASSIGNEE: NORDI C VACCI NE AS 2009

PATENT NUMBER: WO 2009/16085 PATENT DATE: 20090903 WPI ACCESSION NO.: 2009-N26027 (200961)
PRI CRI TY APPLI C. NO.: DK 2008691 APPLI C. DATE: 20080519

PRIORITY APPLIC. NO.: DX 2008691 APPLIC. DATE: 20080519
NATIONAL APPLIC. NO.: WO 2009DK50047 APPLIC. DATE: 20090227
LANGUAGE: English

- New vaccine composition comprises immune stimulating complex, saccharide antigen and aluminum containing adjuvant, used for preparing medicament for treating clinical condition, e.g. bacteremia, meningitis, and pneumonia, in an individual pharmaceutical composition comprising immune stimulating complex, saccharide antigen and aluminum containing adjuvant, useful as vaccine for treatment and prevention of bacteraema, meningitis and...
- ... ABSTRACT: with at least one carrier protein designated carrier protein A; (b) at least one saccharide antigen attached to a carrier protein designated carrier protein B; and (c) at least one aluminum...
- ... Por B (from Neisseria meningitidis), Haemophilus influenzae protein D (PD) heat shock protein, Plasmodium flaciparum pfg27, lactate dehydrogenase peptide, glycoprotein (gp120) of HIV, pertussis proteins, cytokines, lymphokines, artificial proteins comprising multiple human CD4+ T cell epitopes from various pathogen derived antigens, pneumococcal surface protein, iron uptake proteins, serum proteins, immunoglobulins and hormones. Preferably, the carrier protein...
- ...from tetanus toxin, diphtheria toxin, Pseudomonas aeruginosa exotoxin A, toxin A and toxin B of Costridium difficile, tetanus toxoid, fragment C of tetanus toxoid, diphtheria toxoid, pertussis toxoid, pneumolysin. Mutations of pneumolysin...
- ... with lower toxicity. Additionally, the carrier protein A is selected from lipopeptides, Hepatitis B surface antigen (HBsAg) and variants of HBsAg sharing at least 70% sequence identity with HBsAg of SEQ...
- ... carrier protein A is incorporated into the immune stimulating complex. The at least one saccharide antigen is derived from a microbial organism It is derived from encapsulated bacteria. Preferably, it is
- ... Haemophilus influenza type B or from Streptococcus pneumoniae. One or more different Streptococcus pneumonia saccharide antigens are attached to carrier protein B, and where each dosage unit of the vaccine composition comprises at the most 1 mu g of each of the Streptococcus pneumonia saccharide antigens. At least one saccharide antigen is derived from Neisseria meningitides, group B Streptococcus, or derived from Salmonella enterica. The vaccine composition comprises more than one different saccharide antigen, where at least 50-90% of the saccharide antigens are derived from encapsulated bacteria. All saccharide antigens are derived from encapsulated bacteria. The composition comprises 2-200 different saccharide antigens are derived from lencapsulated bacteria. The composition comprises 2-200 different saccharide antigens are derived from general antigens. The all uminum containing adjuvant is selected from all uminum pot assium sulfate (AlK (SO4) 2), al uminum sodium.
- ... adjuvant to which the immune stimulating complex associated with carrier protein A and the saccharide antigen attached to the carrier protein B is adsorbed. Preferably, the vaccine composition comprises at least one saccharide antigen derived from Haemophilus influenzae, and where the clinical condition is one or more selected from ..

- ... meningitis, cellulitis, osteomyelitis, epiglottitis and joint infections; the vaccine composition comprises at least one saccharide antigen derived from Neisseria meningitides and where the clinical condition is one or more selected from bacterial meningitis and meningococcal septicemia; the vaccine composition comprises at least one saccharide antigen derived from Group B Streptococcus and where the clinical condition is one or more selected.
- ... and perinatal group B streptococcal (CBS) disease; the vaccine composition comprises at least one saccharide antigen derived from Salmonella enterica Serovar Typhi and where the clinical condition is typhoid fever; the vaccine composition comprises at least one saccharide antigen derived from Salmonella enterica Serovar typhimurium and where the clinical condition is gastroenteritis; or the vaccine composition comprises at least one saccharide antigen derived from Streptococcus pneumoniae and where the clinical condition is one or more selected from ...
- ... encapsulated bacteria. It can also be used for inducing an immune response to the saccharide antigen and to carrier protein A. The composition and methods are useful for treating clinical condition... DESORIPTORS: pharmaceutical comp., immune stimulating complex, saccharide antigen, aluminum containing adjuvant, appl., vaccine, bacteraemia, meningitis, pneumonia therapy, prevention neuroprotective virucide antiinflammatory immunosuppressive antipyretic...

59/3, K/7 (Item 2 from file: 357) DIALCO(R) File 357: Derwent Biotech Res. (c) 2010 Thomson Reuters. All rts. reserv.

0351586 DBR Accession No.: 2004-23878 PATENT
New Clostridium difficile lactate dehydrogenase
polypeptide and nucleic acid, useful for treating Clostridium
difficile infection in humans and animals - for infection
diagnosis and therapy
AUTHOR BUPNIE J P; MATTHEWS R C
PATENT ASSIGNEE: NEUTEC PHARMA PLC 2004
PATENT NUMBER: W2 00485637 PATENT DATE: 20041007 WPI ACCESSION NO.:
2004-737325 (200472)
PRICRITY APPLIC NO.: CB 20036782 APPLIC. DATE: 20030325
NATICNAL APPLIC NO.: W0 2004CB1383 APPLIC. DATE: 20040325
LANGUAGE: English

LANGUAGE: English

New Clostridium difficile lactate dehydrogenase

polypeptide and nucleic acid, useful for treating O ostridium difficile infection in humans and animals - for infection diagnosis and therapy ABSTFACT: DEFNENT ABSTFACT: NOVELTY - A Clostridium difficile lactate dehydrogenase (I) comprises an amino acid sequence

comprising 311 am no acids (SEO ID NO 2), or...
2): (4) a process for producing a polypeptide comprising (I); (5) an antibody or an antigen-binding fragment specific against (I); (6) a method of manufacture of a medicament for the treatment of C difficile infection; (7) a medicament comprising an amount of an antibiotic and an antibody or an antigen-binding fragment specific against (I); (8) a method of treatment of C difficile infection; (9) a diagnostic test method for detecting the presence in a sample of (1...

... test method for detecting the presence in a sample of antibody specific against a C. difficile lacatate dehydrogenase; (11) a diagnostic test kit for performing a diagnostic test method above; and Page 10

- (12) a pharmaceutical pack for the treatment of a C difficile infection comprising an amount of an antibitic and an antibody or an antigen-binding fragment specific against (I). BIOTECHNOLOGY Preparation (claimed): Producing a polypeptide comprising the C. difficile lactate dehydrogenase comprises culturing the host cell for the production of the polypeptide and recovering the polypeptide...
- ... vector in proper orientation and correct reading frame so that a polypeptide comprising the C. difficile lactate dehydrogenase may be expressed by a cell transformed with the vector. The isolated nucleic acid molecule...
- ...to a promoter sequence. Preferred Method: Manufacturing a medicament for the treatment of a C. difficile infection comprises the use of an antibody or an antigen-binding fragment specific against a C. difficile infection comprises at ministering to a patient in need an amount of an antibiotic and an antibody or an antigen-binding fragment specific against a C. difficile lactate dehydrogenase. The antibiotic is vancomycin, ramplanin, teicoplanin, or metronidazole. The infection is due to C. difficile. The bacterium is also resistant to treatment by the antibiotic alone. Detecting the presence in a sample of a C. difficile lactate dehydrogenase comprises: (a) contacting the sample with an antibody or an antigen-binding fragment specific against the C. difficile lactate dehydrogenase; (b) detecting any antibody-antigen binding reaction; and (c) correlating the results of detection in (b) with the presence of the C. difficile lactate dehydrogenase in the Sample with an antibody or an antigen-binding the sample. Detecting the presence in a sample of antibody-specific against a C. difficile lactate dehydrogenase comprises: (a) contacting the sample with the C. difficile lactate dehydrogenase in the C. difficile lactate dehydrogenase in the sample binding reaction; and (c) correlating the presence in a sample of antibody-antigen binding reaction; and (c) correlating the results of detection in (b) with the presence of antibody specific against the C. difficile lactate dehydrogenase in the sample the sample is a sample from a patient. ACTIVITY Antibacterial. Assays are
- ... but no biological data given. MECHANISM OF ACTION None given. USE The antibody or an antigen-binding fragment, and the medicarment are useful for the treatment or diagnosis of human or animal body. The medicarment is useful for the treatment of a C difficile infection (claimed). The C difficile lactate dehydrogenase and nucleic acid encoding it is useful for the treatment of C difficile infection. EXAMPLE C ostrictium difficile NCTC 11204 was cultured under anaerobic conditions in medium containing 2% (wv) protease peptone...

dehydrogenase isol., antibody, appl. infection diagnosis, therapy bacterium enzyme EC-1.1.1.27 (23, 48)

59/3, K/8 (Item 1 from file: 457) DIALCO(R) File 457: The Lancet (c) 2010 Elsevier Limited. All rights res. All rts. reserv.

0000124934

USE FORMAT 7 OR 9 FOR FULL TEXT
Letters to the editor
Anonymous
The Lancet vol. 348, 9022 PP: 263 Jul 27, 1996 DOCUMENT TYPE:
Page 11

PERIODICAL LANGUAGE: English RECORD TYPE: New, Fulltext LENGTH: 14 Pages WORD COUNT: 14379

ABSTRACT:

and MALT lymphorm of the stormach has been established. 2 Chronic exposure to microorganism related antigens is thought to induce hyperplasia of the MALT from which the neoplastic population develops, and

- ...do not normally bear lymphoid tissue; however, such tissue may appear as a result of antigenic stimulation. Although no association between salivary-gland MALT lymphoma and H pylori infection has yet...
 TEXT:
- ...regression to the mean or artifact may account for the effects of marimast at on cancer antigens. We disagree. The 19 patients they quote are from an abstract prepared 6 months before...
- ...the meeting. Simultaneously, in London, the company released results on 232 patients treated in cancer-antigen trials of similar design in ovarian, pancreatic, prostatic, and colorectal cancers. These studies examined a...consider that longer observation periods are more reliable for determining rates of rise of cancer antigens. We agree. We are aware of temporal variation in cancer-antigen levels. However, in initial clinical trials we were able to justify only 4 weeks treatment...
- ... of sound scientific practice. In the event, we were able to obtain many historical cancer-antigen concentrations and many patients continued treatment after 4 weeks, allowing longer periods of observation. We...

. . . bef or e.

- Our data make it clear that marimastat reduces the rate of rise of cancer antigens in the four types of cancer studied. We are now going on to do a. and MALT lymphoms of the stomach has been established. Or nonic exposure to microorganism related antigens is thought to induce hyperplasia of the MALT from which the neoplastic population develops, and...
- ...do not normally bear lymphoid tissue; however, such tissue may appear as a result of antigenic stimulation. Although no association between salivary-gland MALT lymphoma and Hpylori infection has yet...
- ...mechanisms include direct infection of salivary gland tissue by H pylori or recirculation of organism elated antigens from another site of infection. Because there was no evidence of lymphoma outside of the... substrate saturation and optimum pH. &c) one would expect that I IU of, for example, lactate dehydrogenase (LDH) should catalyse the dehydrogenation of 1 mumol per minute of lactate in the above conditions. This is, however, incorrect: I IU of LDH is usually meant...
- ...is a much lower amount of enzyme than that required to oxidise 1 mumol of lactate per minute to pyruvate; this is attributable to the fact that reaction rates are different...
- ...directions, taking into account the negative change in free energy (Celtadage) in the direction of lactate (Delta dage = 6 kcal/mol). Hence the enzyme unit is different in opposite directions-there...admission was also normal. Faceal cultures were negative for aerobic and microaerophilic bacterial pathogens and Clostridium difficile toxin. Faceal specimens contained some erythrocytes, a few vacuolar B hominis, ...of magnitude. This is an extremely resistant virus that survives water, and in an e antigen positive, chronically infected patient, the virus attains high blood levels. With all these viruses, Page 12

perinatal...drive B-cell proliferation (as in the case of Epstein-Barr virus2), or induce chronic antigen stimulation. Helicobacter pylori,3 herpesvirus (HHV-8), lymphotropic viruses (HTLV-1 and HTLV-11), and... CAPTI ONS:

Figure: Percent change In cancer antigens with different doses of mar I mast at

Figure: Whole-body PET image of a man lying supine...
CLTED REFERENCES:

59/3, K/9 (Item 1 from file: 149) DIALOG(R) File 149: TGG Health&Wellness DB(SM) (c) 2010 Gale/Cengage. All rts. reserv.

03452915 SUPPLI ER NUMBER: 170379830 (USE FORMAT 7 OR 9 FOR FULL TEXT

The HIV-Positive Patient in the ED: HIV/AIDS Update for 2006. Part II. Emergency Medicine Reports, NA April 17,

2006 PUBLICATION FORMAT: Newsletter ISSN: 0746-2506 LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional LINE COUNT: 01163 WORD COUNT: 14418

arterial blood gas, which will show hypoxemia and an increased alveolar-arterial (A-a) gradient. Lactate dehydrogenase (LDH) is elevated in POP, but this has a low specificity and sensitivity for POP ...the meninges, basal ganglia, and cortical gray matter. The most useful test is the cryptococcal antigen test using CSF as it is nearly 100% sensitive and specific. 18 Serum cryptococcal antigen tests also are helpful, but slightly less sensitive. Identification of yeast with India ink staining...

.. The most common opportunistic infections causing acute diarrhea in ALDS patients are Salmonella and C. difficile. Chronic diarrhea is caused by multiple opportunistic including Cryptosporidium parvum, Microsporidia, CMV, and MAC Several . . .

. dose, then 2 mg after each unformed stool, max 16 mg a day). Remember that Clostridium difficile can complicate antibiotic use. While HIV-positive patients are not at higher risk for this bacteria as they are with Salmonella, C. difficile diarrhea occurs frequently as AIDS patients often use antibiotics. Treatment for C. difficile diarrhea is with metronidazole (Flagyl 500 mg PO TID for 10-14 days).

Neoplasms. Kaposi... FNA by polymerase chain reaction (PCR) or HIV culture or tests detecting the p24 HIV antigen should be used in those children younger than 18 months. Of these, HIV culture is...

...lung. Med Clin North Am 1996; 80: 775-801. 17. Quist J, Hill AR. Serum lactate dehydrogenase (LDH) in Pneumocystis carinii pneumonia, tuberculosis, and bacterial pneumonia. Chest 1995; 108; 415-418. 18. . .

59/3, K/10 (Item 2 from file: 149) DI ALOG(R) File 149: TGG Health&Wellness DB(SM) (c) 2010 Gale/Cengage. All rts. reserv.

02936592 SUPPLIER NUMBER: 96416601 (USE FORWAT 7 OR 9 FOR FULL TEXT) Autism, an extreme challenge to integrative medicine. Part II: medical management. (Autism). (Brief Article)

Kidd, Parris M Alternative Medicine Review, 7, 6, 472(28)

Dec. 2002

DOCUMENT TYPE: Brief Article PUBLICATION FORMAT: Magazine/Journal LSSN: 1089-5159 LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Academic: Professional

LINE COUNT: 01466 WORD COUNT: 16634

... mg for a 70 kg adult) were administered with 10 mg/kg/day of magnesium lactate to 11 autistic children for eight weeks; behavior significantly improved and no adverse effects were...contain tryptam ne-like substances. Assays for IAG are not routinely available and are easily contaminated.

Clostridium bacteria that can produce neurotoxins in the intestines can also elevate IAG. A minimally absorbable...

... chronic tetanus infection of the gut as an underlying cause of autismin some individuals. Clostridium tetani is a ubiquitous anaerobic bacterium that is opportunistic in the gut and produces a...or other etiologic triggers; (1) (2) maternal toxic burden, maternal antibodies against the child's antigens, and prenatal contribution to autism risk: (122) (3) interactions between immune or detoxification impairment and...

...intolerances, "leaky gut" -- increased permeability to poorly digested food particles, peptides, microbial toxins, and other antigenic and metabolically active subst ances

Liver: impaired detoxification capacity, often with low cysteine. taurine, or glutathione...

... 6, 68) and others (69)

- * PKU variants
- * 5- Phosphori bosyl pyr ophosphate deficiency
- * Fragile X * Inosine 5-phosphate dehydrogenase weakness
- * Histidinem a/Histidinuría
- * Lesch-Nyhan di sease
- * Adenosi ne deam nase (ADA) weakness
- * Adenyl osucci nat e I yase defici ency
- * ADA binding protein weakness
- 5'-Nucleotidase superactivity
- * Dihydroyrim dine dehydrogenase deficiency

Table 4. Nutrient Supplementation for Heavy Metal Detoxification in Autistic Individuals (28)

* A hypoal I er geni c. . . 2000; 15: 429- 435.

(72.) Gorbach SL, Chang TW Goldin B. Successful treatment of relapsing Clostridium difficile colitis with Lactobacillus GG. Lancet 1987; 2: 1519.

(73.) Reichelt KL, Hole K. Hamberger A...

... children with autistic disorder. J Pediatr 1999; 135: 559-563. (81.) Bolte ER. Autism and Clostridium tetani. Med Hypotheses 1998; 51: 133-144.

(82.) Babarczy E. Szabo G. Telegdy G. Effects...

59/3, K/11 (Item 3 from file: 149)

DIALOG(R) File 149: TGG Health&Wellness DB(SM) (c) 2010 Gale/Cengage. All rts. reserv.

SUPPLI ER NUMBER: 17231887 (USE FORMAT 7 OR 9 FOR FULL TEXT) Phase II trial of (super 131) I-B1 (anti-CD20) antibody therapy with autologous stem cell transplantation for relapsed B cell lymphomas.
Press, Civer W; Eary, Janet F; Appel baum, Frederick R; Martin, Paul J;
Nelp, Wil B; Genn, Stephan; Fisher, Darrell R; Porter, Bruce; Matthews,
Dana C; Cooley, Ted; Bernstein, Irwin D. The Lancet, v346, n8971, p336(5) August 5, 1995

PUBLICATION FORMAT: Magazine/Journal ISSN: 0099-5355 LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDI ENCE: Professional WORD COUNT: 4332 LINE COUNT: 00378

IV disease, nine stage III disease, and one had stage II disease. 11 had increased lactate dehydrogenase concentrations (>250 U/L). Patients had been heavily pretreated, receiving a mean of three different...m nor infections occurred in five patients; three cases of Herpes simplex stomatitis, one case of Clostridium difficile colitis, two Staphylococcus epidermidis catheter infections, and one case of staphylococcal cystitis. Three patients contracted...

from several institutions have reported encouraging response rates with radiolabelled monoclonal antibodies targeting various surface antigens expressed on haematological mal i gnanci es. (21) (22) (23) (24) (25) (26) (27) (28) (29) (30) (31... monocl onal

antibody CKB7 in patients with non-Hodgkin's lymphoma: effects of tumor burden and antigen expression. J Qlin Chccl 1990; 8:792-803. (23) Vriesendorp HM, Herbst JM, Germack MA. . .

59/3. K/12 (Item 1 from file: 444) DIALOG(R) File 444: New England Journal of Med. (c) 2010 Mass. Med. Soc. All rts. reserv.

00127794

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Transmission of Lymphocytic Choriomeningitis Virus by Organ Transplantation (Original Articles)

Fischer, Staci A.; Graham, Mary Beth; Kuehnert, Matthew J.; Kotton, Fischer, Staci A.; Granam, Mary Bern, Ruennert, Matthew J.; Kotton, Camille N.; Srinivasan, Arjun, Marty, Francisco M.; Comer, James A.; Guarner, Jeannette; Paddock, Christopher D.; DeMeo, Dawn L.; Shieh, Win-Ju; Erickson, Bobbie R.; Bandy, Utpala, DeMaria, Alfred, Jr.; Davis, Jeffrey P.; Delmonico, Francis L.; Pavlin, Boris; Likos, Anna; Vincent, Martin J.; Sealy, Tara K.; Goldsmith, Cynthia S.; Jernigan, Daniel B.; Rollin, Pierre E.; Packard, Michelle M.; Patel, Mitesh, Rowland, Courtney; Helfand, Rita F.; Nichol, Stuart T.; Fishman, Jay A.; Ksiazek, Thomas; Zaki, Sherif R.; the LCW in Transplant Recipients Investigation Team The New England Journal of Medicine

May 25, 2006; 354 (21), pp 2235-2249

WORD COUNT: 08371 LINE COUNT: 00606

...blood, and stool were negative, as were studies of the stool for leukocytes, owa, parasites, Gostridium difficile, giardia, cryptosporidium, Yersinia enterocolitica, and rotavirus. Tacrolimus was discontinued because of concern about the worsening...

...administered for suspected acute graft rejection. Fever and hypotension Page 15

persisted, with increases in am notransferase and lactate dehydrogenase levels. The cause of his multiorgan failure was unclear. He had a cardiac arrest and...

...red and hematoxylin counterstain; monoclonal anti-LCW antibody). Panel C shows immunohistochemical staining of LCW antigens in lung tissue from the lung recipient (monoclonal anti-LCW antibody). The image in Panel

...infiltrates in the liver recipient (hematoxylin and eosin). Panel E shows immunohistochemical staining of viral antigens in the transplanted liver (monoclonal anti-Lassa virus antibody). Panel F shows immunohistochemical staining of LOW antigens in the donor kidney of Kidney Recipient 1 (monoclonal anti-LCOW antigens). Panel G shows immunohistochemical staining of viral antigens in the skin of Kidney Recipient 2 (monoclonal anti-Lassa virus antibody). All micrographs are.

... Hamster, and Organ Recipients in the 2005 Quster Red staining indicates the presence of LOW antigens. The image in Panel A contains no immunohistochemical evidence of LOW in choroid plexus from the donor. Panel B shows antigens in the kidney tubules of the donor's household hamster. Panel C shows LOW antigens in lung tissue obtained at autopsy from the lung recipient; there are extensive hyaline-membrane formation and viral antigens in the interstitium Panel D shows LCMV antigens in liver tissue obtained at autopsy from the liver recipient; viral antigens delineate the hepatocyte cytoplasmic membrane. Panel E shows LOW antigens in a kidney specimen obtained at autopsy from Kidney Recipient B; viral antigens in endothelial cells are entering and exiting the glomerulus. Panel F shows LOW antigens in a colon sample obtained at autopsy from Kidney Recipient B, with viral antigens in the muscularis mucosae and mucous cells of colonic glands. Panel G shows LOW antigens in a kidney-biopsy specimen from Kidney Recipient A, who survived; viral antigens are in endothelial cells of the renal interstitium (The studies shown in Panels A, B...foci in multiple tissues, with a notable absence of inflammatory infiltrates and viral inclusions. LOW antigens present in some tissues (e.g., the gastrointestinal tract and skin) correlated with clinical symptoms (e.g., diarrhea and erythema or pustular rash, respectively). Antigens were identified in the leptomeninges of some patients in both clusters. However, signs of meningeal...

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00126734

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Case 25-2005: A 40-Year-Old Man with Prolonged Fever and Weight Loss (Case Records of the Massachusetts General Hospital)

Kasper, Dennis L.; Sahani, Dushyant; M sdraji, Joseph. The New England Journal of Medicine Aug 18, 2005; 353 (7),pp 713–722

LINE COUNT: 00389 WORD COUNT: 05368

TEVT

...presence of IgG antibodies to Epstein-Barr virus (EBV) latent membrane protein and EBV nuclear antigen were positive; those for IgM anti-EBV antibodies, hepatitis B antigen and antibody, and antimitochondrial antibodies were negative. Antinuclear antibodies were present at a titer of

... became increasingly abnormal. Alkaline phosphatase rose to a very high level, and the level of lactate dehydrogenase was high, with ongoing elevation of hepatocellular enzymes. The erythrocyte sedimentation rate continued to rise...

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00123694

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Weekly Clinicopathological Exercises: Case 14-2003: A 73-Year-Old Woman with Pneumonia and Progressive Pespiratory Failure (Case Records of the Massachusetts General Hospital)

Waxman, Aaron B.; Shepard, Jo-Anne O.; Mark, Eugene J. The New England Journal of Medicine May 8, 2003; 348 (19), pp 1902-1912 LINE COUNT: 00569 WCPD COUNT: 07864

TFXT

- ...am notransferase, and alkaline phosphatase were normal. Ceftriaxone and azithromycin were administered intravenously. A test for Clostridium difficile toxin was negative, and an examination of the stool showed no leukocytes, ova, or parasites... Two sputum specimens contained a few neutrophils, with no microorganisms. Tests for adenovirus antigen and for parainfluenza virus types 1, 2, and 3 antigens were normal. The result of a test for legionella microorganisms was pending. A right-sided
- ...deciliter; globulin, 0.6 g per deciliter), the amylase level 10 U per liter, the lactate dehydrogenase level 127 U per liter, and the pH 7.40; a culture was sterile. Vancomycin...
- ...the sediment contained 3 to 5 red cells per low-power field. Tests for C. difficile toxin and for protozoal and helm nthic ova in the stool were negative. A blood culture...The results of many additional tests were pending. Another stool specimen was positive for C. difficile toxin, and trimethoprim sulfamethoxazole was given...titer of 1:128 or higher suggests acute legionellosis. A highly sensitive and specific urinary-antigen test is available to detect L. pneumophila serogroup 1 in patients with pneumonia. This organism accounts for approximately 70 per cent of L. pneumophila infections, and antigens from the organism persist in the urine for weeks after the initiation of antimicrobial therapy...the biopsy specimen were negative for legionella, chlanydia, mycoplasma, and mycobacteria. A test for legionella antigen in the urine was negative. The common causes of bronchiolitis obliterans with organizing pneumonia are...

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00123646

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Weekly Clinicopathological Exercises: Case 13-2003: A 14-Month-Old Boy with Hepatomegaly, Perianal Lesions, and a Bony Lump on the Forehead (Case Records of the Massachusetts General Hospital)

Usmani, G. Naheed; Westra, Sjirk J.; Younes, Souhad. The New England Journal of Medicine Apr 24, 2003; 348 (17),pp 1692-1701 LINE COUNT: 00550 WCFD COUNT: 07601

...bowel disease. A liquid stool specimen showed no protozoal or helminthic ova; a test for Clostridium difficile toxin was negative, and a stool culture grew normal enteric flora. An upper gastrointestinal series

...due to small, subcutaneous, bluish, nontender tumor nodules, which are usually seen in infants. The lactate dehydrogenase level is invariably elevated at the time of the diagnosis. Because the typical features of.

... consistent with the presence of a lymphoma, the indirect biochemical markers -- his low level of lactate dehydrogenase and normal level of uric acid -- are not.

Acut e Mvel oi d Leukemi a

Patients with acute myeloid...and dendritic-cell neoplasms. It is now recognized as a neoplasm of Langerhans' cells, the antigen-presenting dendritic cells that typically reside in the epiderm's. A study of the X-linked...

... combination of morphologic and immunophenotypic features. The gold standard is the expression of CD1a, an antigen expressed by normal Langerhans' cells and immature thymic T cells; S-100 protein is also...

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00120876

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Weekly Clinicopathological Exercises: Case 35-2000: An 82-Year-Old Woman with Bilateral Adrenal Masses and Low-Grade Fever (Case Records of the Massachusetts General Hospital)

Udelsman, Robert; Dong, Henry Y. The New England Journal of Medicine Nov 16, 2000; 343 (20), pp 1477-1483 LI NE COUNT: 00403 WORD COUNT: 05570

TEXT

.. began to pass three or more loose stools daily, without bleeding. A stool specimen contained Clostridium difficile toxin; another antibiotic was prescribed, and a repeated test for C. difficile toxin was negative. The diarrhea subsided. The cataract extraction was uneventful, and she returned to...adrenal insufficiency may present with gastrointestinal symptoms, hyponatremia, hyperkalemia, and hypotension. (Ref. 3,35) The lactate dehydrogenase level is often, but not Page 18

al ways, el evated. (Ref. 30,33,35) Increased skin pigmentation has...stains on a frozen-section specimen revealed staining of the cells for the B-cell antigen CD20 (recognized by antibody L26) and for the leukocyte common antigen (CD45). The cells lacked detectable surface immunoglobulin heavy and light chains and cytokeratin. Both the...

...at the time of presentation, which indicates extensive adrenal destruction, and a high level of lactate dehydrogenase.

...the adrenal masses decreased to about a quarter of their initial size. The level of lactate dehydrogenase became almost normal but then began to increase. The patient subsequently had bilateral facial Bell

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00120115

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Weekly Clinicopathological Exercises: Case 7-2000: A 23-Year-Old Man with Hemolytic Anemia and Bloody Diarrhea (Case Records of the Massachusetts General Hospital)

Cliff, Ira A.; Compton, Carolyn C. The New England Journal of Medicine Mar 9, 2000; 342 (10), pp 722-728

LINE COUNT: 00472 ' WORD COUNT: 06526

TEXT

...no ova or parasites, a stool culture yielded no intestinal pathogens, and a test for Clostridium difficile toxin was negative. On further questioning, the patient reported no history of arthralgia, or al ulcers...that are helpful in evaluating the anema include the marked reticul coytosis, the hyperbilirubinema, the elevated lactate dehydrogenase level, and the decreased haptoglobin level, which are diagnostic of hemolytic anema. Findings on the...to oxidative hemolysis of the Heinz-body type, especially in patients with glucose-6-phosphate dehydrogenase deficiency affecting the red cells. (Fef. 28...

...red cells, (Fef. 23) but it has been hypothesized that absorption of non-red-cell antigens across the diseased colonic mucosa leads to the production of antibodies that cross-react with...

...type, it is especially difficult to accept the proposed pathogenetic relation between transcolonic absorption of antigens and the production of anti-erythrocyte autoantibodies...

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00118182

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Weekly Clinicopathological Exercises: Case 19-1998: A 70-Year-Old Man with Diarrhea, Polyarthritis, and a History of Reiter's Syndrome (Case Records of the Masachusetts General Hospital)

Shmerling, Robert H.; Caliendo, Angela M

Page 19

The New England Journal of Medicine Jun 18, 1998; 338 (25),pp 1830-1836

LINE COUNT: 00500 WORD COUNT: 06912

TEXT

...were the levels of urea nitrogen, creatinine, glucose, uric acid, calcium, phosphorus, magnesium electrolytes, and lactate dehydrogenase. The results of other laboratory tests are shown in Tables i and 2. "Table 1...s syndrome, but other microbes have been implicated, including group A streptococcus, Staphylococcus aureus, campylobacter, Gostridium difficile, intestinal parasites, and mycobacterial species...

...use rather than by true infection. There are rare reports of reactive arthritis after C. difficile colitis. (Pef. 19) The dental work may have exposed the patient to bacterial antigens that provoked reactive arthritis, but his antibiotic treatment was apparently adequate, and such antigens seldom cause reactive arthritis...cause the disorder. Serum sickness, an immunologic reaction after exposure to medications or other foreign antigens, can cause fever and arthritis but is usually accompanied by rash and arthralgia rather than...infectious cause, with cultures of blood and stool and testing for the toxin of C. difficile. The guidelines include an algorithm for oligoarthralgia, which specifies joint aspiration early in the evaluation.

...At a clinicopathological conference, it is tempting to favor a rare disease such as C. difficile reactive arthritis, but I have approached this patient as I would in clinical practice. Even...monocytes. Routine bacterial culture of the fluid was negative. A positive enzyme immunoassay for C. difficile toxin established the diagnosis.

...Pathogenic strains of C. difficile produce two toxins. Toxin A is an enterotoxin that causes intestinal inflammation with mucosal damage...

... symptoms in humans. (Pef. 35) Toxin B is not enterotoxic in animals. (Pef. 36) C. difficile can be identified in stool specimens with the use of a variety of methods, including...

...The organism was named ``difficile'' because it was considered difficult to grow. With strict anaerobic conditions and a selective medium

...not a reliable diagnostic test. Also, 2 percent of healthy adults are colonized with C. difficile, so the presence of the organism may not be correlated with disease. (Fef. 38) Latex-agglutination tests can detect the bacterial enzyme glutamate dehydrogenase, but they have a low sensitivity and lack specificity because of cross-reaction with other...

...37,39,40) In addition, the tests cannot distinguish toxigenic from nontoxigenic strains of C difficile, since both types of strains produce the enzyme...

...et al. (Ref. 46) described a patient who had chronic Reiter's syndrome and C. difficile reactive arthritis...

.The pathogenesis of C. difficile reactive arthritis is unclear. Other enteric pathogens causing a reactive arthritis are locally invasive, theoretically allowing bacterial antigenic components to enter the systemic circulation, (Ref. 45) which leads to an immunologic reaction in the joints. Although C. difficile is not locally invasive, toxin A increases intestinal permeability, which may allow bacterial antigenic components to penetrate the intestinal wall. (Ref. 45) Patients with HLA-B27 have increased bowel permeability, (Ref. 50) which may have a role in the pathogenesis of C. difficile reactive arthritis...

.. used to treat the arthritis and are usually combined with antibiotics to treat the C. difficile infection. The long-term prognosis for patients with C. difficile reactive arthritis is good, but in the patient described by Cope et al., (Ref. 46... ... Anat om cal Di agnosi s

C. difficile reactive arthritis...

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00117523

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Weekly Clinicopathological Exercises: Case 35-1997: A 65-Year-Old Woman with a Dry Cough and Pulmonary Nodules (Case Records of the Massachusetts General Hospital)

Faling, L. Jack; Mark, Eugene J. The New England Journal of Medicine Nov 13, 1997; 337 (20), pp 1449-1458 LINE COUNT: 00537 WORD COUNT: 07421

TEXT

heart and mediastinum appeared normal. A stool culture yielded no near and need as finding bear of brinds. A stool cutturely led by the pathogens, and a test for Clostridium difficile was negative. Additional laboratory tests were performed. Tests for rheumatoid factor and anti-double-stranded. Table 4. On the next day, the reticul ocyte count was 3_6 percent, and the lactate dehydrogenase level was normal. A CT scan of the abdomen revealed minimal hyperdensity of the liver... admission, appeared to be noninfectious, with negative stool cultures and a negative assay for C. difficile toxin. Although this assay is not 100 percent sensitive, the thickened colon on the CT. . are consistent with the presence of metastatic tumor. The slight elevation of the serum carcinoembryonic antigen level is nonspecific and could have been due to inflammatory bowel disease. The widespread pulmonary... Other patients have an acute presentation simulating pneumonia. Leukocytosis and an elevated level of serum lactate dehydrogenase are common, and hyperglobulinemia may be present. (Ref. 19) Although the erythrocyte sedimentation rate is...

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00115805

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Weekly Clinicopathological Exercises: Case 19-1996: Multisystem Failure in a 33-Year-Od Man after Bone Marrow Transplantation (Case Records of the Massachusetts General Hospital)

Miller, Kenneth B.: Graeme-Cook, Filona M. The New England Journal of Medicine Jun 20, 1996; 334 (25), pp 1655-1662

...hepatitis C surface antibody, and hepatitis C antibody. Tests were negative for hepatitis B surface antigen, toxoplasma, syphilis, human T-cell lymphotropic virus type 1, and the human immunodeficiency virus. | * Table. . .

...patient ate little and vomited bloody liquid; total parenteral nutrition was initiated. Tests for cytomegal ovir us antigenemia and Clostridium difficile toxin were negative. Low-dose dopamine was administered. On the 14th hospital day, mucositis was...his appetite returned. A test for urinary eosinophilia was negative. A test for cytomegal ovirus early antigen was negative. On the 30th day, an erythematous rash was prominent over the trunk, and.

...disclosed an extensive neutrophilic infiltrate. The direct and total bilirubin, aspartate am notransferase, alanine aminotransferase, and lactate dehydrogenase levels rose progressively, despite the resumption of treatment with methylprednisolone in high doses...his previous renal allograft. The previous allograft may have sensitized the patient to minor histocompatibility antigens, thus explaining the severe graft-versus-host disease. Hyperacute graft-versus-host disease is an... MIIer: With a prior solid-organ transplant, the host may be sensitized to minor histocompatibility antigens; such sensitivity would increase the risk of graft-versus-host disease and the toxic effects

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Weekly Clinicopathological Exercises: Case 17–1996: A 48-Year-Old Man with the Acquired Immunodeficiency Syndrome, Abdominal Pain, and Bloody Diarrhea (Case Records of the Massachusetts General Hospital)

Ives, David V.; Smith, R. Neal. The New England Journal of Medicine May 30, 1996; 334 (22), pp 1461-1467 LINE COUNT: 00473 WORD COUNT: 06539

TEVI

...was believed to be due to aspiration. A buffy-coat specimen was positive for cytomegal ovirus antigen (60 white cells per 150,000). When foscarnet was substituted for ganciclovir, the patient's...

- ...of stool specimens showed no white cells, acid-fast bacilli or other pathogenic microorganisms, or Clostridium difficile toxin...
- ...The white-cell count was 19,400 per cubic millimeter. A blood test for cytomegalovirus antigen was positive (18 white cells per 150,000). Films of the abdomen showed a markedly...
- ...contained white and red cells. A culture yielded no pathogenic microorganisms. A test for C. difficile toxin was positive. Metronidazole was administered orally.|*Figure 1.-Abdominopelvic CT Scan Chained Six Days...
- ...bowel sounds. Laboratory tests were performed (Tables 1 and 2). A blood test for cytomegal ovirus antigen was positive (27 white cells per 150,000). A radiograph of the chest showed bibasilar...nitrogen concentration fell to 16 mp per deciliter (5.7 mmol per liter), and the lactate dehydrogenase concentration rose to 236 U per liter. Padiographs of the abdomen continued to show nodular...cytomegal ovirus colitis (which is related to HIV infection or other causes of immunocompromise) and C difficile colitis (which is of nosocomial origin) -- could explain much of his presentation. This would be a severe Page 23

and hemorrhagic presentation of cytomegalovirus colitis, however, and the C difficile colitis was responding to appropriate antibiotic therapy, with a partial resolution of the toxin-mediated... Pseudomembranous colitis caused by C difficile toxin could explain most, if not all, of the findings in this case. At least three events must occur for C difficile to result in colitis: alteration of the normal bowel flora (usually by broad-spectrum antibiotics with activity against anaerobes), colonization of the gut by C difficile (usually as a result of nosocomal transmission), and growth of C difficile with elaboration of fits two toxins. The colonic mucosal involvement has three stages: epithelial necrosis...

...This patient had received antibiotics for two episodes of pneumonia. C. difficile colitis has been reported in patients with HIV infection when the only antibiotic used was...

...once daily as prophylaxis against pneumocystis pneumonia. (Ref. 26) Colonization of the bowel with C. difficile may have occurred during a previous hospital admission or by contact with a long-term...

...this possible source of exposure to the organism is not mentioned in the history. C difficile toxin was documented in the patient's stool several days before this admission, and he...count of over 50,000 per cubic millimeter in an immunocompetent adult with severe C difficile diarrhea. (Pef. 27) C difficile colitis may cause acute megacol on and perforation, as well as life-threatening diarrhea. (Pef. 28,29) The response of C difficile colitis to either metronidazole or oral vancomycin may be delayed by the continued administration of ...

...packed red cells and platelets, despite appropriate antibiotic therapy for both cytomegalovirus infection and C. difficile colitis. The failure of this therapy does not rule out these diagnoses, in view of...

...pathological examination showed evidence of both severe cytomegalovirus colitis and pseudomembranous colitis caused by C. difficile infection. Although I would not be surprised to find a third or even a fourth...

... Clinical Diagnosis Colitis due to cytomegalovirus and Clostridium difficile infections...

... Pseudomembranous colitis caused by Clostridium difficile infection...that were weakly adherent to the mucosa and formed a pseudomembrane -- findings consistent with C. difficile infection (Fig. 4). Acid-fast bacilli, fungi, and pneumocystis were not identified.] Figure 4.-Mucosal.

...x350) *.**FIQUEE CM TTED**| *Figure 6. -Multiple Endothelial Cells in the Lamina Propria Stained for Cytomegal ovirus Antigen (ImmunoperoxidaseStain, x350) *.**FIQUEE CM TTED...

...enteric pathogens, including hemorrhagic E. coli H7:C157, with normal enteric flora; tests for C. difficile toxins A and B were also negative. In a patient with a positive test for C. difficile toxin, these findings are diagnostic of pseudomembranous colitis associated with C. difficile infection, since pseudomembranes may persist for at least two weeks after the toxin has become...

...Cytomegal ovirus antigen was identified several times in cytospin preparations of peripheral blood cells in this case by immunoperoxidase staining for cytomegal ovirus intermediate early antigen. (Fief. 36,37) in addition, large, atypical infected cells were identified that may have Page 24

been. . .

- ...C. difficile is the causative agent in most cases of pseudomembranous colitis and approximately 20 percent of...
- diarrhea. Pseudomembranes are most prominent in the patients who have the most severe symptoms. C. difficile can be cultured in 3 percent of healthy adults, 2 to 11 percent of hospitalized.
- ...receiving antibiotics or chemotherapy, who have altered or diminished flora, the natural resistance to C. difficile colonization is absent. The mechanism of this resistance is unclear, but other clostridial anaerobes or...are most commonly seen in the capillary endothelium (Ref. 42) Cytomegalovirus increases HLA class II antigens, induces an as-yet uncharacterized procoagulant activity, and causes the adherence of neutrophils to endothelial...
- .. conclusion, pseudomembrane formation in colitis is most commonly associated with toxin-producing infections by C. difficile. However, pseudomembrane formation is a common pathologic pathway for a variety of toxic or infectious...
- Anatomical Diagnoses
- Pseudomembranous colitis associated with toxin-producing C. difficile infection and cytomegalovirus colitis...

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00112424

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Weekly Clinicopathological Exercises: Case 4-1994; A 38-Year-Old Man with ALDS and the Recent Onset of Diarrhea, Hematochezia, Fever, and Pulmonary Page 25

Infiltrates (Case Records of the Massachusetts General Hospital)

Basgoz, Nesli; Mattia, Anthony R. The New England Journal of Medicine Jan 27, 1994; 330 (4),pp 273-280 LINE COUNT: 00611 WOHD COUNT: 08434

TEXT
...in earlier years, and more recently he switched to cigars. He had glucose-6-phosphate dehydrogenase deficiency; a painful peripheral neuropathy was ascribed to HiV infection. He was all lergic to sulfadiazine ...for cold agglutinins, stool examinations for ova and parasites, assay of a stool specimen for Costridium difficile toxin, repeated examination of induced sputum specimens for P. carinii and acid-fast bacilli, a test for legionella antigen, and microscopical examination of a stained stool specimen for acid-fast bacilli were negative.

... was positive (323 U on enzyme-linked immunosorbent assay), and a test for cytomegalovirus early antigen was negative. Multiple cultiure specimens, including the skin and bone marrow biopsy specimens, were negative. I the buttooks. Pancytopenia, hyponatremia, moderately elevated aspartate aminorransferase and alkaline phosphatase levels, a markedly elevated lactate dehydrogenses level, and hypoalbuminemia with hyporglobulinemia were found. Arterial-blood gas evaluation revealed an elevated alveolar...

...The typical clinical presentation includes cough, fever, and dyspnea, with a bliateral infiltrate, an elevated lactate dehydrogenase level, and hypoxemia. Several other radiologic patterns have also been reported, including a more reticulonodular...

... with lymphadenopathy and pleural effusions. Peticuloendothelial-cell hyperplasia can be seen, and a markedly elevated lactate dehydrogenase level is a prominent laboratory finding (Pef. 10). Clinically apparent gastrointestinal involvement is very uncommon... their HV infection. The diagnosis is greatly aided by assays that detect a cryptococcal capsular antigen in body fluids by latex-agglutination techniques (Pef. 23). This patient's course is not.

explained by cryptococcal infection. I shall assume that he had a negative test for cryptococcal antigen.

bloopsy specimens, or skin lesions. In addition, a radioimmunoassay.

...biopsy specimens, or skin lesions. In addition, a radioimmunoasse to a major H capsulatum polysaccharide antigen correlates well with disseminated infection (Fef. 36). Biopsies may show granulomas with caseation, but such... A radioimmunoassay for histoplasma polysaccharide antigen appears to be useful for the rapid diagnosis of disseminated disease.

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immunosorbent assays for detection of Histoplasma capsulatum polysaccharide antigen. J Infect Dis 1989; 160: 678-85.

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Weekly Clinicopathological Exercises: Case 36-1992: Abrupt Development of Cardiac Enlargement and Respiratory Distress in a 31-Year-Old Man with AIDS (Case Records of the Massachusetts General Hospital)

Kamitsuka, Paul F.; Southern, James F. The New England Journal of Medicine Sep 10, 1992; 327 (11), pp 790-799 LINE COUNT: 00669 WORD COUNT: 09232

.. of a specimen of the fluid disclosed no fungi; serologic tests for syphilis and cryptococcal antigen and a culture were negative. A stool culture and a test on a stool specimen for Clostridium difficile toxin were negative. Diphenoxylate hydrochloride-atropine sulfate was administered for diarrhea, with improvement...the gastrointestinal tract, the liver, and the bone marrow (Ref. 2-7). The elevated lactic dehydrogenase level in the patient under discussion raises this diagnostic possibility, although this enzyme is elevated... biopsy specimen of lung tissue. Blood and urine cultures may be positive, and serum cryptococcal antigen is detected in 75 to 99 percent of HIV-infected patients with disseminated disease. C...

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 Silverman BA, Rubinstein A. Serum lactate dehydrogenase levels in adults and children with acquired immune deficiency syndrome (AIDS) and AIDS-related complex...

(Item 13 from file: 444) 59/3, K/24 DIALCO (R) File 444: New England Journal of Med. (c) 2010 Mass. Med. Soc. All rts. reserv.

00108922

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Weekly Clinicopathological Exercises: Case 29-1991: A 56-Year-Old Woman With Pneumoperitoneum Three Months After Receiving A Renal Transplant (Case Records of the Massachusetts General Hospital)

Scully, Robert E.; Mark, Eugene J.; McNeely, William F.; McNeely, Betty U.

The New England Journal of Medicine Jul 18, 1991; 325 (3), pp 183-195

LINE COUNT: 01070 WORD COUNT: 14767

...alanine aminotransferase (ALAT) 60 U (new normal for a woman, 7 to 30), and the lactate dehydrogenase (LDH) 540 U per liter (new normal, 110 to 210). Another specimen of arterial blood... Another colonic process that can lead to pneumoperitoneum is far advanced colitis produced by Clostridium difficile. This disorder is associated with

Page 27

therapy with antibiotics, including the cephal osporins, which this patient received...turmor. Immunoperoxidase stains on frozen sections of the turmor showed staining for the leukocyte common antigen (CD45), confirming the hematopoletic lineage of the cells. The majority of the cells also expressed...

...of cells with plasmacytoid differentiation. In normal lymphoid differentiation to plasma cells, pan-B-cell antigens on the cell surface, such as CD20, are lost, and therefore the malignant lymphoid cells

59/3, K/25 (Item 14 from file: 444)
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00102849

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Case 8-1987: A 44-Month-Cld Girl with Fever of Unknown Origin after Repair of the Tetralogy of Fallot (Case Records of the Massachusetts General Hospital)

Kevy, Sherwin V.; Mark, Eugene J. The New England Journal of Medicine February 19, 1987; 316 (8), pp 466-475 LINE COUNT: 00821 WORD COUNT: 11330

TEXT

... A stool culture yielded no enteric pathogens, and a test on a stool specimen for Clostridium difficile toxin was negative. A test on the serum for cytomegalovirus antibodies was positive: tests for...

...Tests for antinuclear antibodies and rheumatoid factor were negative, and a skin test with candida antigen was negative at 48 hours. Another echocardiogram revealed no evidence of pericardial effusion or vegetations...4 degreesC. Increasing rhinorrhea and cough were observed. The urine was again normal. The lactic dehydrogenase (LDH) was 444 U per liter. Pepeated blood cultures and culture of a urine specimen... Secondly, of all the laboratory results the most meaningful was the elevation of the Serumlactate dehydrogenase (LDH) level.

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00102336

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Case 39 1986. A 66-Year-Old Woman with Fever, Fluctuating Neurologic Signs, and Negative Blood Cultures (Case Pecords of the Massachusetts General Hospital)

.Beal, M Flint; Ferry, Judith A. The New England Journal of Medicine October 2, 1986; 315 (14), pp 874-885 LINE COUNT: 00937 WORD COUNT: 12936

TEXT

...The bilirubin was 0.5 mg per 100 ml (9 micromole per liter). The lactic dehydrogenase (LDH) was 717 U per liter (normal, 84 to 186). A Page 28

specimen of arterial blood...dioxide 22 mml per liter. The serum aspartate am notransferase (SCOT) was 11 U, the lactic dehydrogenase (LDH) 359 U, the creatine kinase (CX) less than 5 U, and the alkaline phosphatase...

- ... of stained specimens showed no microorganisms or malignant-tumor cells; a test for cryptococcal polysaccharide antigen and a culture were negative. A serologic test for syphilis, direct and indirect Coorbs' tests, and tests for antinuclear antibodies, rheumatoid factor, and hepatitis B surface antigen and antibody were negative. The CH50 was 205 U per milliliter; the C3 was 105...negative. A tuberculin skin test (5 TU) was negative, and a skin test with mumps antigen was positive. An echocardiogram revealed normal values, good left ventricular function, and no evidence of...
- ...culture was negative. On the following day diarrhea recurred. Assay of a stool specimen for Clostridium difficile toxin was negative, and a culture yielded no enteric pathogens. On the eighth hospital day... immune complexes in the bloodstream. Thirty percent of the patients have an associated hepatitis B antigenemia, (Pei: 17, 21) a feature not found in this case. The CT findings consist of...of laboratory values include mild anemia, an elevated erythrocyte sedimentation rate, a very high serum lactate dehydrogenase level, and an elevated protein content in the cerebrospinal fluid (Peir. 52). Penal involvement may...
- ...normal endothelial cells and clearly neoplastic cells, have been described (Pef. 55). Factor VIII-associated antigen has been demonstrated by immunoperoxidase techniques, (Pef. 52,54,56) but some investigators have advised...were performed on both frozen and paraffin-embedded sections. Immunoperoxidase staining for factor VIII-associated antigen was positive for endothelial cells. Staining of the intralum nal tumor cells was negative, however, providing...
- ... Staining of the turror cells was strongly positive, on the other hand, for common leukocyte antigen (Fig. 4). Staining of the cells present within the lurren was also faintly but definitely positive for Bi, a B-lineage antigen; thus, the malignant-turror cells were of B-lymphocyte origin. Finally, the perivascular small lymphocytes...
- ... of the B-immunoblastic type. *Figure 4. Positive Stain of Intraluminal Cells for Common Leukocyte Antigen (Immunoperoxidase Method, x 500)
 *. **FIGURE CM TTED. ..
- ...tissue sections showed that the intravascular tumor cells reacted with antibody to the leukocyte common antigen and lacked lysozyme and chloroacetate esterase, markers of myeloid cells. Cur experience, coupled with that.
- ...In the case under discussion the presence of a B-cell associated surface antigen (B1) and the absence of T-cell associated antigens suggest a B-lineage neoplasm Frozen tissue was not available in the other three cases. Both our patients had a mild cerebrospinal fluid pleocytosis, as in this case. Factor VIII antigen was not present on the surface of the malignant-tumor cells in the one case in which we examined for this antigen.

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22. Bron KM...

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